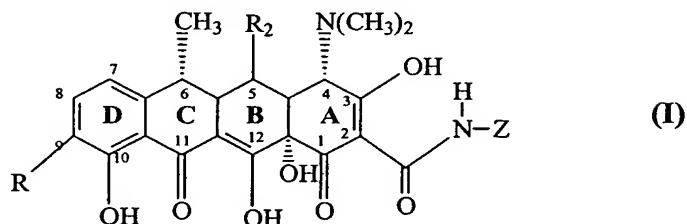


Claims***What is claimed is:***

1. A 5,9-substituted tetracycline.

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2. A compound of claim 1 of the following Formula I:



wherein R is alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an aryalkyl;

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R² is alkanoyl; aroyl; alkaroyl; carbocyclic aryl, heteroaromatic, alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an aryalkyl;

Z is hydrogen, alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; aryalkyl, carbocyclic aryl, heteroalicyclic or heteroaromatic group; and pharmaceutically acceptable salts thereof.

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3. A compound of claim 1 that is

5-propionate-9-t-butyl doxycycline;

9-chloro-t-butyl-5-propionate doxycycline;

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9-t-butyl-6-alpha-deoxy-5-oxy-tetracycline;

9-t-butyl-5-oxytetracycline;

9-t-butyl-6-alpha-deoxy-5-formyloxy-tetracycline;

9-t-butyl-6-alpha-deoxy-5-acetoxy-tetracycline;

9-t-butyl-6-alpha-deoxy-5-propionyloxy-tetracycline;

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9-t-butyl-6-alpha-deoxy-5-phenylcarbonyloxy-tetracycline;

9-t-butyl-6-alpha-deoxy-5-benzylcarbonyloxy-tetracycline;

9-t-butyl-6-alpha-deoxy-5-dimethylaminocarbonyloxy-tetracycline;

9-t-butyl-6-alpha-deoxy-5-cyclopentylcarbonyloxy-tetracycline;

9-t-butyl-6-alpha-deoxy-5-cyclobutylcarbonyloxy-tetracycline;

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9-t-butyl-6-alpha-deoxy-5-cyclohexylcarbonyloxy-tetracycline;

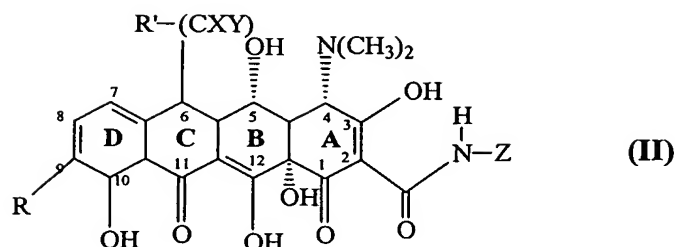
9-t-butyl-6-alpha-deoxy-5-cycloheptylcarbonyloxy-tetracycline;

9-(chloro-t-butyl)-6-alpha-deoxy-5-oxy-tetracycline;

- 9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-oxy-tetracycline;
 9-(amino)-t-butyl-6-alpha-deoxy-5-oxy-tetracycline;
 9-[(piperidino)-t-butyl]-6-alpha-deoxy-5-oxy-tetracycline;
 9-[(diethylamino)-t-butyl]-6-alpha-deoxy-5-oxy-tetracycline;
 5 9-[(dipropylamino)-t-butyl]-6-alpha-deoxy-5-oxy-tetracycline;
 9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-formyloxy-tetracycline;
 9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-acetoxy-tetracycline;
 9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-propionylcarbonyloxy-tetracycline;
 9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-phenylcarbonyloxy-tetracycline;
 10 9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-benzylcarbonyloxy-tetracycline;
 9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-dimethylaminocarbonyloxy-
 tetracycline;
 9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-cyclopentylcarbonyloxy-
 tetracycline;
 15 9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-cyclobutylcarbonyloxy-
 tetracycline;
 9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-cyclohexylcarbonyloxy-
 tetracycline; or 9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-
 cycloheptylcarbonyloxy-tetracycline; and pharmaceutically acceptable salts
 20 thereof.
4. The compound of claim 2 wherein R is alkyl having 1 to about 20 carbon atoms;
 alkenyl having 2 to about 20 carbon atoms; alkynyl having 2 to about 20 carbon
 atoms; alkoxy having 1 to about 20 carbon atoms; alkylthio having 1 to about 20
 25 carbon atoms; alkylsulfinyl having from 1 to about 20 carbon atoms;
 alkylsulfonyl having from 1 to about 20 carbon atoms; alkylamino having from 1
 to about 20 carbon atoms; or aryalkyl;
 R² is alkyl having 1 to about 20 carbon atoms; alkenyl having 2 to about
 20 carbon atoms; alkynyl 2 to about 20 carbon atoms; alkoxy 1 to about 20
 30 carbon atoms; alkylthio having 1 to about 20 carbon atoms; alkylsulfinyl having
 from 1 to about 20 carbon atoms; alkylsulfonyl having from 1 to about 20 carbon
 atoms; alkylamino having from 1 to about 20 carbon atoms; or aryalkyl; alkanoyl
 from 1 to about 20 carbon atoms; aroyl; alkaroyl; carbocyclic aryl,
 heteroaromatic; and
 35 Z is hydrogen, alkyl having 1 to about 20 carbon atoms; alkenyl having 2
 to about 20 carbon atoms; alkynyl 2 to about 20 carbon atoms; alkoxy 1 to about
 20 carbon atoms; alkylthio having 1 to about 20 carbon atoms; alkylsulfinyl

having from 1 to about 20 carbon atoms; alkylsulfonyl having from 1 to about 20 carbon atoms; alkylamino having from 1 to about 20 carbon atoms; aryalkyl; carbocyclic aryl, or an heteroalicyclic group.

- 5 5. The compound of claim 2 wherein R is alkyl having 1 to about 12 carbon atoms; alkenyl having 2 to 12 about carbon atoms; alkynyl having 2 to 12 about carbon atoms; alkoxy having 1 to about 12 carbon atoms; alkylthio having 1 to about 12 carbon atoms; alkylsulfinyl having 1 to about 12 carbon atoms; alkylsulfonyl having 1 to about 12 carbon atoms; alkylamino having 1 to about 12 carbon atoms; or benzyl;
- 10 R² is alkyl having 1 to about 12 carbon atoms; alkenyl having 2 to 12 about carbon atoms; alkynyl having 2 to 12 about carbon atoms; alkoxy having 1 to about 12 carbon atoms; alkylthio having 1 to about 12 carbon atoms; alkylsulfinyl having 1 to about 12 carbon atoms; alkylsulfonyl having 1 to about 12 carbon atoms; alkylamino having 1 to about 12 carbon atoms; benzyl; aroyl; alkaroyl; carbocyclic aryl, heteroaromatic; and Z is hydrogen.
- 15
6. The compound of claim 2 wherein R and/or R² is selected from the group consisting of t-butyl; chloro-t-butyl; (dimethylamino)-t-butyl; propionate; piperidinoethyl; formyloxy; acetoxy; propionyloxy; phenylcarbonyloxy; benzylcarbonyloxy; piperidino; amino; diethylamino; dipropylamino; acetylcarbonyloxy; propionylcarbonyloxy; phenylcarbonyloxy; benzylcarbonyloxy; dimethylaminocarbonyloxy; cyclopentylcarbonyloxy; cyclobutylcarbonyloxy; cyclohexylcarbonyloxy; cycloheptylcarbonyloxy; and Z is hydrogen.
- 20
- 25
7. The compound of claim 1, wherein said compound is selected from the group consisting of 5-propionate-9-t-butyl doxycycline; 9-t-butyl-6-deoxy-5-propionylcarbonyloxytetracycline, 9-t-butyl-6-deoxy-5-acetylcarbonyloxytetracycline, 9-t-butyl-6-deoxy-5-cyclobutylcarbonyloxytetracycline, and pharmaceutically acceptable salts thereof.
- 30
8. A 9,13-substituted tetracycline compound.
- 35 9. A compound of claim 8 that is of the following Formula II:



wherein R is alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an aryalkyl;

R¹ is hydrogen, hydroxy, alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an aryalkyl;

X and Y are each independently hydrogen; halogen; hydroxyl; cyano, sulfhydryl; amino; alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an aryalkyl;

Z is hydrogen, alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; aryalkyl, carbocyclic aryl, heteroalicyclic or heteroaromatic group; and pharmaceutically acceptable salts thereof.

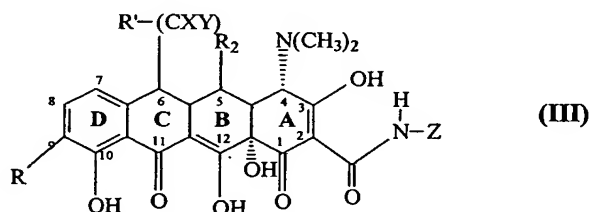
10. A compound of claim 8 that is:

- 13-cyclopentylthio-9-t-butyl-5-oxy-tetracycline;
- 13-methylthio-9-t-butyl-5-oxy-tetracycline;
- 13-ethylthio-9-t-butyl-5-oxy-tetracycline;
- 13-propylthio-9-t-butyl-5-oxy-tetracycline;
- 13-isopropylthio-9-t-butyl-5-oxy-tetracycline;
- 13-butylthio-9-t-butyl-5-oxy-tetracycline;
- 13-isobutylthio-9-t-butyl-5-oxy-tetracycline;
- 13-pentylthio-9-t-butyl-5-oxy-tetracycline;
- 13-isopentylthio-9-t-butyl-5-oxy-tetracycline;
- 13-cyclobutylthio-9-t-butyl-5-oxy-tetracycline;
- 13-cyclopentylthio-9-t-butyl-5-oxy-tetracycline;
- 13-cyclohexylthio-9-t-butyl-5-oxy-tetracycline;
- 13-phenylthio-9-t-butyl-5-oxy-tetracycline;
- 13-(3,4-dichlorophenyl)thio-9-t-butyl-5-oxy-tetracycline;
- 13-benzylthio-9-t-butyl-5-oxy-tetracycline;
- 13-(4-chlorobenzyl)thio-9-t-butyl-5-oxy-tetracycline;
- 13-(3,4-dichlorobenzyl)thio-9-t-butyl-5-oxy-tetracycline;
- 13-(4-methoxybenzyl)thio-9-t-butyl-5-oxy-tetracycline;

13-(2,3-dihydroxypropyl)thio-9-t-butyl-5-oxy-tetracycline; and
 5-propionate-13-cyclopentylthio-9-t-butyl oxytetracycline;
 5-propionate-13-cyclopentylthio-9-piperidinoethyl oxytetracycline;
 and pharmaceutically acceptable salts thereof.

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11. A 5,9,13-substituted tetracycline.
12. A compound of claim 11 that is of the following Formula III:



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wherein R is alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl;
 alkylsulfonyl; alkylamino; or an aryalkyl;

R² is alkanoyl; aroyl; alkaroyl; carbocyclic aryl, heteroaromatic, alkyl;
 alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an
 aryalkyl such as benzyl;

15

X and Y are each independently hydrogen; halogen; hydroxyl; cyano,
 sulfhydryl; amino; alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl;
 alkylsulfonyl; alkylamino; or an aryalkyl;

Z is hydrogen, alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl;
 alkylsulfonyl; alkylamino; aryalkyl, carbocyclic aryl, heteroalicyclic or
 heteroaromatic group; and pharmaceutically acceptable salts thereof.

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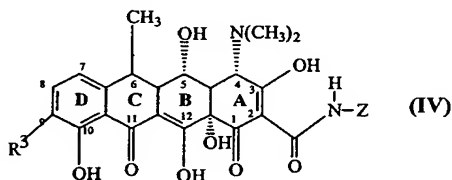
13. A compound of claim 11 that is:
- 13-cyclopentylthio-9-t-butyl-5-formyloxy-tetracycline;
 13-methylthio-9-t-butyl-5-acetoxy-tetracycline;
 13-ethylthio-9-t-butyl-5-propionylcarbonyloxy-tetracycline;
 13-propylthio-9-t-butyl-5-butanylcarbonyloxy-tetracycline;
 13-isopropylthio-9-t-butyl-5-cyclopentylcarbonyloxy-tetracycline;
 13-butylthio-9-t-butyl-5-cyclohexylcarbonyloxy-tetracycline;
 13-isobutylthio-9-t-butyl-5-cycloheptylcarbonyloxy-tetracycline;
 13-pentylthio-9-t-butyl-5-formyloxy-tetracycline;
 13-isopentylthio-9-t-butyl-5-acetoxy-tetracycline;
 13-cyclobutylthio-9-t-butyl-5-propionylcarbonyloxy-tetracycline;

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- 13-cyclopentylthio-9-t-butyl-5-cyclopentanylcabonyloxy-tetracycline;
 13-cyclohexylthio-9-t-butyl-5-cyclohexylcabonyloxy-tetracycline;
 13-phenylthio-9-t-butyl-5-phenylacetylcarbonyloxy-tetracycline;
 13-cyclopentylthio-9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-formyloxy-
 5 tetracycline;
 13-cyclopentylthio-9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-acetoxy-
 tetracycline;
 13-cyclopentylthio-9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-
 propionylcarbonyloxy-tetracycline;
 10 13-cyclopentylthio-9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-
 phenylcarbonyloxy-tetracycline;
 13-cyclopentylthio-9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5 -
 benzylcarbonyloxy-tetracycline;
 13-cyclopentylthio-9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-dimethylamino
 15 carbonyloxy-tetracycline;
 13-cyclopentylthio-9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-cyclopentyl
 carbonyloxy-tetracycline;
 13-cyclopentylthio-9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-cyclobutyl
 carbonyloxy-tetracycline;
 20 13-cyclopentylthio-9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-S-cyclohexyl
 carbonyloxy-tetracycline; or
 13-cyclopentylthio-9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-cycloheptyl
 carbonyloxy-tetracycline; and pharmaceutically acceptable salts thereof.

- 25 14. A compound of the following Formula IV:



wherein R^3 is alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl;
 alkylsulfonyl; alkylamino; or an aryalkyl;

- 30 Z is hydrogen, alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl;
 alkylsulfonyl; alkylamino; aryalkyl, carbocyclic aryl, heteroalicyclic or
 heteroaromatic group; and pharmaceutically acceptable salts thereof.

15. A compound of claim 14 which is

9-t-butyl tetracycline;

9-t-butyl anhydrotetracycline;

9-t-butyl minocycline; and pharmaceutically acceptable salts thereof.

- 5 16. The compound of claim 14 wherein R^3 is alkyl having 1 to about 20 carbon atoms; alkenyl having 2 to about 20 carbon atoms; alkynyl having 2 to about 20 carbon atoms; alkoxy having 1 to about 20 carbon atoms; alkylthio having 1 to about 20 carbon atoms; alkylsulfinyl having from 1 to about 20 carbon atoms; alkylsulfonyl having from 1 to about 20 carbon atoms; alkylamino having from 1 to about 20 carbon atoms; or aryalkyl; and

10 Z is hydrogen, alkyl having 1 to about 20 carbon atoms; alkenyl having 2 to about 20 carbon atoms; alkynyl 2 to about 20 carbon atoms; alkoxy 1 to about 20 carbon atoms; alkylthio having 1 to about 20 carbon atoms; alkylsulfinyl having from 1 to about 20 carbon atoms; alkylsulfonyl having from 1 to about 20 carbon atoms; alkylamino having from 1 to about 20 carbon atoms; aryalkyl; carbocyclic aryl, or an heteroalicyclic group.

17. The compound of claim 14 wherein R^3 is alkyl having 1 to about 12 carbon atoms; alkenyl having 2 to 12 about carbon atoms; alkynyl having 2 to 12 about carbon atoms; alkoxy having 1 to about 12 carbon atoms; alkylthio having 1 to about 12 carbon atoms; alkylsulfinyl having 1 to about 12 carbon atoms; alkylsulfonyl having 1 to about 12 carbon atoms; alkylamino having 1 to about 12 carbon atoms; or benzyl; and Z is hydrogen.

- 25 18. The compound of claim 14 wherein R^3 is selected from the group consisting of t-butyl; chloro-t-butyl; (dimethylamino)-t-butyl; methylcyclohexyl; methylcyclobutyl; methylpentyl; bromomethylpentyl; nitromethylpentyl; and acetoxymethylpentyl.

- 30 19. The compound of claim 14, wherein said compound is selected from the group consisting of 9-t-butyl-6-deoxy-5-hydroxytetracycline, 9-[1'-(1'-methyl)cyclohexyl]-6-deoxy-5-hydroxytetracycline, 9-[1'-(1'-methyl)cyclopentyl]-6-deoxy-5-hydroxytetracycline, 9-[1'-(1'-methyl)cyclobutyl]-6-deoxy-5-hydroxytetracycline, 9-[2'-(2'-methyl)pentyl]-6-deoxy-5-hydroxytetracycline, 9-[4'-(1'-bromo-4'-methyl)pentyl]-6-deoxy-5-hydroxytetracycline, 9-[4'-(1'-dimethylamino-4'-methyl)pentyl]-6-deoxy-5-hydroxytetracycline, 9-[4'-(1'-pyrrolidinyl-4'-methyl)pentyl]-6-deoxy-5-
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- hydroxytetracycline, 9-[4'-(1'-cyano -4'-methyl)pentyl]-6-deoxy-5-hydroxytetracycline, 9-[4'-(1'-nitro -4'-methyl)pentyl]-6-deoxy-5-hydroxytetracycline, 9-[4'-(1'-acetoxy -4'-methyl)pentyl]-6-deoxy-5-hydroxytetracycline); 9-t-butyl tetracycline; 9-t-butyl anhydrotetracycline; 9-t-butyl minocycline; and pharmaceutically acceptable salts thereof.
- 5
20. A method for treating against a targeted microorganism comprising administering to the microorganism a compound of claim 1.
- 10 21. A method for treating against bacteria comprising administering to the bacteria a compound of claim 1.
22. A method for treating a mammal suffering from or susceptible to a microorganism infection or disease associated therewith comprising administering to the mammal a compound of claim 1.
- 15
23. A method for treating a mammal suffering from or susceptible to bacteria infection comprising administering to the mammal a compound of claim 1.
- 20 24. The method of claim 22 wherein the mammal is a human.
25. The method of claim 22 wherein the microorganism or bacteria is tetracycline sensitive.
- 25 26. The method of claim 22 wherein the microorganism or bacteria is tetracycline resistant.
27. The method of claim 21 wherein the bacteria is *E. coli.*, *S. aureus* or *E. faecalis*.
- 30 28. A method for converting tetracycline resistant bacteria into tetracycline resistant bacteria, comprising
- a) contacting the resistant bacteria with a predetermined quantity of a compound of claim 1, and
- b) concomitantly administering to the bacteria a predetermined quantity of a tetracycline-type compound that is different than the compound of step a).
- 35
29. A pharmaceutical composition of claim 1.